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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,465	06/20/2001	Josee Hamel	55190-044	9640

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EXAMINER	
FORD, VANESSA L	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,465	HAMEL ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5 November 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,19,25 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19,25 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *3/17/04* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's response filed November 5, 2003. Claims 1-17, 20-24 and 26-33 have been cancelled. Claims 18, 25 and 34 have been amended.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

3. The rejection following rejections are withdrawn in view of Applicant's amendment and response:

a) Rejection of claims 34 under 35 U.S.C., 101, page 4, paragraph 3, of the previous Office action.

b) Rejection of claim 18 under 35 U.S.C. 112, second paragraph, page 10, paragraph 6, of the previous Office action.

c) Rejection of claim 18 under 35 U.S.C. 112, second paragraph, page 10, paragraph 7, of the previous Office action.

d) Rejection of claim 18 under 35 U.S.C. 112, second paragraph, page 10, paragraph 8 of the previous Office action.

e) Rejection of claims 18-19, 25 and 34 under 35 U.S.C., 102(b), pages 11-12, paragraph 9, of the previous Office action.

Rejections Maintained

4. The rejection of claims 18-19, 25 and 34 under 35 U.S.C. 112, first paragraph (written description) is maintained for the reasons set forth on pages 4-7, paragraph 4 of the previous Office Action.

The rejection was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses SEQ ID NO: 332 (elected sequence), which correspond to an isolated protein from *Streptococcus pneumoniae*. The claims are directed to encompass amino acid sequences that correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:332 (elected sequence), the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in

> the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a protein requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself." Id. at 1170, 25 USPQ2d at 1606.

Therefore, only SEQ ID NO: 332 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant urges that the specification provides written description of the claimed chimeric polypeptides, vaccines and their use. Applicant urges that the specification teaches how to generate chimeric polypeptides and specifically discloses fragments of BVH3 and BVH-11 polypeptides that have at least 95% identity with BVH-3 or BVH-11, the two components of the chimeric polypeptide.

Applicant's arguments filed November 5, 2003 have been fully considered but they are not persuasive. The specification fails to provide written description for polypeptides that have 95% similarity to the elected sequence (SEQ ID NO. 332). Although applicant asserts that the specification teaches polypeptides that are 95% similar to BVH-3 and BVH-11 (which are the two components of the chimeric polypeptide) it does not provide written description for polypeptides that are 95% similar

to the elected sequence (SEQ ID NO.332). In the absence of such support the rejection is maintained.

4. The rejection of claims 18-19, 25 and 34 under 35 U.S.C. 112, first paragraph (enablement) is maintained for the reasons set forth on pages 5-10, paragraph 5 of the previous Office Action.

The rejection was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated *Streptococcus pneumoniae* polypeptide that has the amino acid sequence as set forth in SEQ ID NO: 332 (elected sequence), does not reasonably provide enablement for epitope bearing portions of the polypeptide having the amino acid sequence as set forth in SEQ ID NO: 332.

The claims are directed to encompass amino acid sequences that correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification teaches that the antigenic/immunogenic fragments of invention include one or more epitopic regions (page 15). The specification does not disclose, which amino acids are involved in the claimed epitope bearing portions of the *Streptococcus pneumoniae* polypeptide as set forth in SEQ ID NO:332 nor does the specification provide guidance as to how many location changes (i.e. deletions) can be used to produce an epitope bearing portion of SEQ ID. NO:332. No working examples are shown containing the missing information. There is no guidance provided as to which amino acids can be deleted and still have the epitope retain its biological function. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of epitopes broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species.

Without such information, one of skill in the art could not predict which deletions, would result in the desired epitope. Since the amino acid sequence of the protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the protein's structure relates to function. However, the problem of the prediction of protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations

to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to epitope bearing portions of a polypeptide has an amino acid sequence as set forth in SEQ ID NO:332 having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make of the claimed *Streptococcus pneumoniae* polypeptide in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

The Applicant has not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of deletions and epitopes of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the protein's structure and still maintain activity is unpredictable and the experimentation left those skilled in the art is unnecessarily and improperly, extensive and undue. See Amgen Inc v Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S. P.Q. 546(Bd. Pat=. App & int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention commensurate in scope with the claims.

Applicant urges that the specification provides amino acid sequences, methods of generating the claimed chimeric polypeptides, methods for generating the claimed vaccines and methods of their use. Applicant urges that the specification also provides data to evidence the effectiveness of the claimed vaccine. Applicant urges that the

specification provides sufficient guidance to the skilled practitioner to make and use the claimed invention.

Applicant's arguments filed November 5, 2003 have been fully considered but they are not persuasive. The specification fails to provide enablement for polypeptides that have 95% similarity to the elected sequence (SEQ ID NO. 332). Although the specification teaches polypeptides that have similarity to BVH-3 and BVH-11 (which are the two components of the chimeric polypeptide) it does not provide enablement for polypeptides that are 95% similar to the elected sequence (SEQ ID NO.332). In the absence of such support the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 18-19 and 25 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 in particular, recites "at least about". It is unclear as to what Applicant is referring. Clarification is required.

6. Claim 34 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 34 recites "susceptible to". It is unclear as to what Applicant is referring. Clarification is required.

Status of Claims

7. No claims allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Vanessa L. Ford
Biotechnology Patent Examiner
February 12, 2004

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